

REMARKS

Applicant has discovered that DNA molecules encoding polypeptides having protein kinase domains activate stress signaling in plants. Expression of such isolated genes in plants leads to the production of genetically-engineered plants having increased tolerance to environmental stress. The invention therefore has significant implications for increasing yields and improving the quality of plant products.

Election/Restriction

Applicants affirm their election, without traverse, of Group I, claims 1-7, 24-26, and 36-46, and have canceled the remaining claims 8-23, 27-35, and 47-48.

Office Action

Claim 36 stands rejected under 35 U.S.C. § 101. Claims 1-7, 24-26, 36-39, and 41-46 stand rejected under 35 U.S.C. § 112, first paragraph. Claims 5-7 and 36-46 stand rejected under § 112, second paragraph. Claims 36-46 stand rejected under 35 U.S.C. § 102(b). Claims 1-7, 24-26, and 36-46 stand rejected under 35 U.S.C. § 103(a). Each of these rejections is addressed as follows.

Rejection Under 35 U.S.C. § 101

Claim 36 was rejected under 35 U.S.C. § 101 because the claimed invention was deemed directed to non-statutory subject matter. Applicant respectfully notes that claim

36 is directed to “substantially pure DNA” compositions. This term is defined, for example, at page 7 (line 19) - page 8 (line 2) as DNA that is free of the genes which, in the naturally-occurring genome of the organism from which the DNA of the invention is derived, flank the gene. In view of this definition, applicant points out that these compositions are not found in nature and, therefore, constitute statutorily patentable subject matter. Given this clarification, this rejection should be withdrawn.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-7, 24-26, 36-39, and 41-46 stand rejected, under 35 U.S.C. § 112, first paragraph, on the basis that the disclosure in applicant’s specification (1) fails to provide a written description of the claimed invention and (2) is not commensurate in scope with the claimed invention. For the following reasons, each of these rejections is respectfully traversed.

Written Description

Claims 1-7, 24-26, 36-39, and 41-46 stand rejected, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to convey to one skilled in the art that the inventor had possession of the claimed invention. Applicant respectfully traverses this basis of the rejection.

The adequate written description requirement of 35 U.S.C. § 112, ¶ 1 provides that the specification shall contain a written description of the

invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same...

The written description requirement serves “to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; how the specification accomplishes this is not material.” *In re Wertheim*, 541 F.2d 257, 262, 191 U.S.P.Q. 90, 96 (C.C.P.A. 1976). In order to meet the written description requirement, the applicant need not utilize any particular form of disclosure to describe the subject matter claimed, but “the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.” *In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989) (citation omitted). Stated another way, “the applicant must . . . convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention.” *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 U.S.P.Q.2d 1111, 1117 (Fed. Cir. 1991).

The claimed invention encompasses methods for protecting plants against an environmental stress involving the expression of DNA molecules encoding polypeptides that include a protein kinase (PK) domain (claims 1-7); plants (and seeds and cells thereof) including DNA molecules encoding polypeptides that include a PK domain (claims 24-26); and substantially pure DNAs encoding polypeptides consisting essentially of a PK domain, wherein expression of such polypeptides increases the level

of tolerance to an environmental stress in a transgenic plant and cells including such DNA molecules (claims 36-46).

Applicant's specification explicitly describes to the skilled worker what is claimed, that is, (i) methods for producing plants that are tolerant to an environmental stress (e.g., drought), (ii) genes encoding polypeptides encoding PK domains, and (iii) methods for isolating and identifying DNAs useful for practicing the claimed invention. For example, the inventor explicitly describes methods for producing stress tolerant plants at pages 10-11 and 36-37 of the specification. The inventor also describes, for example, at pages 16-22, not only a stress-signaling expression pathway, but also expression constructs useful for generating plants having tolerance to an environmental stress. Moreover, with respect to isolating genes encoding polypeptides that consist essentially of a PK domain, the inventor explicitly describes (see, for example, Fig. 3C) several PK domains, and also explicitly describes to persons skilled in the art how to select PK domains active in stress signaling, for example, by utilizing the disclosed transient maize protoplast system, described, for example, at pages 13-15.

Together, this description provides one skilled in the art with exemplary PK domains and genetic constructs, as well as methods of using kinase domains to engineer plants that are tolerant to an environmental stress. Clearly, the inventor was in possession of the claimed invention at the time the application was filed and provided a written description that readily enables the skilled worker to identify plants and genes falling within the claimed subject matter. Applicant's specification therefore satisfies

the written description requirement of § 112. This rejection may be withdrawn.

Enablement

Claims 1-7, 24-26, and 36-46 also stand rejected under § 112, first paragraph based on the assertion that the teaching of applicant's specification is not commensurate in scope with the present claims. The rejection essentially turns on the assertions that practicing the claimed method of protecting plants against an environmental stress would require trial and error experimentation, and that it would also require trial and error experimentation to determine whether the claimed genes, when expressed in a plant, would confer increased tolerance to an environmental stress. This rejection should be withdrawn.

As an initial matter, applicant wishes to address the Examiner's specific concern that applicant has "not shown if any DNA molecule would confer tolerance in transgenic plants to environmental stress." On this point, applicant directs the Examiner's attention to the Declaration of Jen Sheen, the sole inventor on this application. Dr. Sheen points out that, as outlined in the patent application, the PK domain of AtCDPK1 was placed under the control of the 35S promoter (as described in the specification, for example, at pages 16-19). This expression construct was then introduced into wild-type *Arabidopsis* using standard *Agrobacterium*-mediated transformation methods. Dr. Sheen next compared non-transformed wild-type plants with transgenic plants expressing the PK domain for drought tolerance by withholding water for 10 days. As Dr. Sheen points out, wild-type (non-transformed) plants wilted, but transgenic plants constitutively

expressing the PK domain of AtCDPK1 failed to wilt and remained healthy. These data provide compelling evidence that transgenic plants constitutively expressing a polypeptide that includes a PK domain are tolerant to environmental stresses, such as drought, when compared to corresponding non-transformed plants. Accordingly, there is no reasonable basis for doubting the objective truth of statements found in applicant's specification regarding enablement or predictability of the present invention. *In re Marzocchi*, 439 F.2d 220, 224, 169 U.S.P.Q. 367, 370 (C.C.P.A. 1971).

With respect to isolating additional PK-domain encoding genes, applicant notes that the specification, for example, at pages 16-20, and as depicted in Figs. 3B and 3C, provides clear guidance, using specific examples, that may be utilized for identifying and isolating a variety of DNA sequences encoding polypeptides having PK domains, from a variety of sources. In addition, the specification at pages 22-24, under the heading "Isolation of Regulators of the Stress Signal Transduction Response," provides general guidance on the routine methods known at the time the application was filed for identifying and characterizing the gene sequences required by the claims. Such standard methods described in the specification include: (1) the design and utilization of oligonucleotides for cloning, (2) hybridization cloning methodologies, (3) library screening procedures, and (4) PCR-based amplification cloning strategies. Together these methods, alone or in combination, are effective for isolating and cloning desired DNAs.

Once a gene sequence is isolated, the specification also provides methods for

generating expression constructs using the isolated DNAs and testing whether such constructs activate stress-signaling pathways. For example, at pages 24-31 and at pages 36-37, under the heading “Expression Constructs Encoding Regulators of the Stress Signal Response,” the specification provides clear instructions about how to express such sequences in plants, and how to test whether the sequences express a polypeptide that regulates stress signaling. In one particular example, genes encoding a polypeptide having a PK domain may be readily tested for activating stress signaling using applicant’s disclosed protoplast transient expression system, as described in the specification, for example, at pages 13-14. In this system, a construct expressing a polypeptide having a PK domain is coexpressed with a reporter construct (e.g., *HVA1-GFP*), and genes expressing PK domains that activate reporter gene expression are quickly identified as positive regulators of stress signaling. Once identified, such genes are then used to confer tolerance to an environmental stress *in planta*, exactly as described for the experiments discussed by Dr. Sheen for the PK domain of the AtCDPK1 polypeptide. Alternatively, if desired, isolated DNAs may be tested directly in plants to confirm their ability to confer tolerance to an environmental stress.

In addition to the techniques, all of the tools for expressing these DNA molecules were known when applicant filed the patent application. Exemplary expression vectors, promoters, and terminators are described in the specification, for example, at pages 28-29, and at pages 30-31. Moreover, the specification, for example, at pages 31-36 describes several methods for introducing the vectors into plant cells, and for

regenerating transformed plants. Plants expressing these genes may then be selected, for example, by visual examination (e.g., wilting). Indeed, the data provided in Dr. Sheen's declaration provides strong evidence that plants expressing a polypeptide having a PK domain have an increased tolerance to environmental stress. Given these exemplary teachings and results, applicant's specification cannot be found as failing to enable the claimed invention when the techniques required to practice the invention are disclosed in the specification and available to those skilled in the art. See *In re Wands*, 858 F.2d 731, 740, 8 USPQ2d 1400, 1406; *In re Strahilevitz*, 668 F.2d 1229, 1232, 212 U.S.P.Q. 561, 563 (C.C.P.A. 1982).

Applicant also directs the Office's attention to the enablement standard as articulated in *In re Wands*, 858 F.2d. 713, 8 U.S.P.Q.2d 1400 (Fed. Cir. 1988). *Wands* involved the identification of monoclonal antibodies of a specific isotype directed against particular antigens. The nature of this technology involved screening hybridomas to identify those that secreted antibody having the desired characteristics. Identifying genes having the desired characteristics according to the present invention, as in *Wands*, involves straightforward and routine screening methods. As was stated in *Wands*, "a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed." Certainly, in applicant's case identifying genes expressing polypeptides having a PK domain useful for practicing the claimed invention cannot constitute undue experimentation, especially given

applicant's teaching of the transient protoplast expression system that identifies genes encoding regulators of the stress signal transduction pathway. Moreover, it is improper to find that such experimentation is "undue" simply because it requires some "trial and error," *W.L. Gore & Assoc. v. Garlock, Inc.* 721 F.2d 1540, 1557, 220 U.S.P.Q. 303, 316 (Fed. Cir. 1983). This is true even when the experimentation is needed to weed out inoperative embodiments. *Atlas Powder v. E.I. DuPont deNemours*, 750 F.2d 1569, 1576-77, 224 U.S.P.Q. 409, 414 (Fed. Cir. 1984).

For the all of the above-mentioned reasons, applicants respectfully request withdrawal of the § 112, first paragraph rejection.

Rejections Under 35 U.S.C. § 112, second paragraph

Claims 5-7 and 36-46 were rejected under § 112, second paragraph as being indefinite on several grounds, which are addressed as follows.

Claim 5 was deemed vague on the basis of reciting the phrase "multiple stress conditions." Applicant traverses this rejection, noting that the specification, for example, at page 9 (line 25) - page 10 (line 1), page 10 (lines 11-12), page 13 (lines 5-6), and page 37 (lines 4-5) indicates clearly that this phrase refers to two or more stress conditions including drought, salinity, or extreme temperature. Moreover, results described in Fig. 1, and the accompanying description found at pages 13-14, elaborate on stress signaling under multiple stress conditions: cold, high salt, dark, and ABA. Given these examples, one skilled in the art would have little difficulty understanding the meaning of this

phrase. Reconsideration on this issue is requested.

Claim 6 was deemed vague on the basis of reciting the phrase “activates the expression of a stress-protective protein.” This rejection has been met by the present amendment to claim 6 that now specifies that the polypeptide “activates the expression of a stress-protective protein-encoding gene.” In addition, applicant notes that the meaning of this phrase is made clear by applicant’s specification. For example, the phrase is readily understood from reading the passages found respectively under the headings “Constitutive AtCDPK1 and AtCDPK1a Activate Stress Signaling” and “CDPK1 Activates But PP2C Abolishes Stress Signaling” at pages 16 and 20. In particular, these passages explain that polypeptides that include a PK domain activate gene expression of stress-inducible proteins. In view of this clarification, it is requested that this § 112, second paragraph rejection be withdrawn.

Claim 7 was deemed vague on the basis of reciting the phrase “constitutively expressed.” Applicant respectfully traverses this ground of rejection.

Applicant notes that the specification provides ample meaning to this phrase. For example, applicant again directs the Office’s attention to page 16 of the specification where, under the heading “Constitutive AtCDPK1 and AtCDPK1a Activate Stress Signaling,” several examples of constitutively expressed genes are provided.

In view of this exemplary passage, a skilled worker would understand the meaning of the phrase in the context of the present invention. Claims need only “reasonably apprise those skilled in the art” as to their scope and be precise as the “subject matter permits.”

Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1385 , 231 U.S.P.Q. 81, 94-95 (Fed. Cir. 1986). Applicant's claim satisfies this standard, and reconsideration on this issue is respectfully requested.

Claims 36 and 40, and dependent claims 37-39 and 41-46 were rejected as indefinite for reciting the word "substantially." This rejection is respectfully traversed.

Applicant first notes that claims 36 and 40 are respectively directed to "substantially pure DNA" and cells that include such "substantially pure DNA." Second, the meaning of "substantially pure DNA" is defined at page 7 (line 19) - page 8 (line 2) of applicant's specification. In view of this definition, applicant contends that one skilled in the art would readily understand the meaning of this phrase, and it is requested that the § 112, second paragraph rejection be withdrawn.

Rejections Under 35 U.S.C. § 102(b)

Claims 36-46 were rejected under 35 U.S.C. § 102(b) as anticipated by Urao *et al.* (Mol. Gen. Genet. 244: 331-340, 1994).

Claim 36, as amended, and claims 37- 46, which refer directly or indirectly to claim 36, are now drawn to a DNA molecule that encodes a polypeptide consisting essentially of a PK domain, as well as to cells that include such DNA molecules. Since Urao *et al.* discloses full-length cDNA molecules encoding CDPK and discloses neither DNA molecules encoding a polypeptide consisting essentially of a PK domain nor cells that include such DNA, this ground for the rejection may be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-7 and 24-26 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Urao *et al.* (Mol. Gen. Genet. 244: 331-340, 1994; “Urao”) taken with Gordon-Kamm *et al.* (Plant Cell 2: 603-618, 1990; “Gordon-Kamm”). In applying this rejection, the Office asserts:

[I]t would have been obvious to combine the teachings Urao *et al.* and Gordon-Kamm *et al.* to obtain a method for protecting [a] plant against an environmental stress by transforming with a recombinant protein kinase (PK) domain-containing gene whereby said plants have an increased tolerance to an environmental stress as claimed. Said transgenic plants are expected to be tolerant to other types of stresses such as salt, dehydration, and temperature the mechanisms of resistance to these stresses share many common pathways. Thus the claimed invention would have been *prima facie* obvious as a whole to one of ordinary skill in the art at the time the invention was made, especially in absence of evidence to the contrary.

For the following reasons, applicant traverses this rejection.

The test of obviousness *vel non* is statutory. It requires that one compare the claim’s “subject matter as a whole” with the prior art “to which said subject matter pertains.” 35 U.S.C. §103(a). The inquiry is fact-specific. This is so “whether the invention be a process for making or a process of using, or some other process.” *In re Kuehl*, 475 F.2d 658, 665, 177 U.S.P.Q. 250, 255 (C.C.P.A. 1973). When the references cited by the Patent Office fail to establish a *prima facie* case of obviousness, the rejection is improper and must be withdrawn. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988).

Applicant’s presently claimed invention stems, at least in part, from the recognition that polypeptides including a PK domain activate stress-signaling pathways

in plants; and that expression of a gene encoding a polypeptide that includes a PK domain confers tolerance to environmental stress. Accordingly, applicant's invention is directed to methods for protecting a plant against an environmental stress by expressing in the plant a DNA molecule encoding a PK domain (claims 1-7); and is directed to plants having an increased level of tolerance to an environmental stress through expression of such DNA molecules (claims 24-26). Because neither Urao *et al.* nor Gordon-Kamm *et al.* disclose or suggest applicant's claimed invention, these references, either alone or in combination, cannot produce the invention, nor render it obvious.

Turning first to Urao *et al.*, this reference fails to disclose that expression of a polypeptide that includes a PK domain confers stress tolerance on a plant. Despite their study of the expression pattern of two genes—AtCDPK1 and AtCDPK2—encoding polypeptides having PK domains, Urao does not even mention or suggest that these genes may be introduced into a plant to confer tolerance to an environmental stress. Despite the agricultural need for generating plants with increased tolerance to environmental stress, Urao simply does not teach, or suggest expressing any gene in any cell for producing such genetically-engineered plants. The slightest mention of even the possibility of using a gene encoding a polypeptide that includes a PK domain for conferring stress tolerance in a plant is simply not found in Urao. Thus, the Office's contention that it would have been obvious to make plants expressing a PK domain to confer tolerance to an environmental stress is incorrect.

In addition, to the extent that the Office relies upon Urao to establish that it would

have been obvious to express a gene that encodes a polypeptide having a PK domain in a plant to provide tolerance to an environmental stress, merely because it would be obvious to try such an experiment, the Office is in error. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 231 U.S.P.Q.2d 81 (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987). (“Obvious to try” is improper consideration in adjudicating obviousness issue.) What is needed for obviousness is a reasonable expectation of success. *In re O’Farrell*, 853 F.2d 894, 7 U.S.P.Q.2d 1673 (Fed. Cir. 1988). As a matter of law, the § 103 rejection based on Urao should be withdrawn.

Similarly, a conclusion that the invention would have been obvious cannot be properly reached when Urao *et al.* is considered in view of Gordon-Kamm *et al.* Gordon-Kamm teaches only a method of plant transformation. Applicant, of course, acknowledges that plant transformation was routine at the time that the invention was made, but this reference does not in any way suggest expressing a DNA molecule encoding a polypeptide that includes a PK domain for engineering stress tolerance, as presently claimed. Gordon-Kamm provides no information on the biology of stress tolerance in plants.

Because Urao *et al.* is limited to teaching *Arabidopsis* CDPKs and fails to teach or suggest engineering stress-tolerant plants by expressing a polypeptide that includes a PK domain in such plants, and further because Gordon-Kamm fails to suggest transforming such genes in plants, the Gordon-Kamm article does not provide a logical predicate for rendering applicant’s claimed invention obvious. Gordon-Kamm adds nothing to Urao

with respect to understanding stress tolerance in plants. Gordon-Kamm does not even mention a single polypeptide that includes a PK domain, and certainly does not suggest that plants could be genetically engineered to express such polypeptides for increasing stress tolerance. Accordingly, Gordon-Kamm *et al.* cannot teach or suggest what they themselves did not know or recognize. The Urao *et al.* and Gordon-Kamm *et al.* references are unavailing, and, in combination, cannot support the present obviousness rejection.

Claims 36-46 also stand rejected under 35 U.S.C. § 103(a) as unpatentable over Urao taken with Gordon-Kamm. For the following reasons, this rejection may be withdrawn.

With respect to this rejection, applicant notes that Urao's characterization of the expression patterns of CDPKs in *Arabidopsis* and Gordon-Kamm's teaching of plant transformation fail entirely to teach or suggest applicant's claimed invention: substantially pure DNA encoding a polypeptide consisting essentially of a PK domain (claims 36-44) or cells that include such DNA (claims 45-46). Indeed if either Urao or Gordon-Kamm had actually considered isolating such genes, and expressing them in cells for generating stress tolerant plants, one or both of these references would have certainly made this point clear. Instead, Urao describes nothing beyond characterizing the expression of AtCDPK1 and AtCDPK2, and Gordon-Kamm never even discusses polypeptides that include a PK domain, much less isolating a gene encoding a polypeptide that consists essentially of a PK domain. Moreover, neither reference so

much as mentions expressing a gene encoding a polypeptide that consists essentially of a PK domain, much less provide a rationale for doing so. And given that Urao only describes the full-length *Arabidopsis* CDPK genes and their expression profiles and Gordon-Kamm only describes transformation of maize, Urao and Gordon-Kamm provide no motivation for isolating the claimed DNA sequences or for expressing such isolated sequences in a cell.

Given that neither Urao nor Gordon-Kamm mention or suggest engineering stress tolerant plants, the Office has failed to explain, when analyzing the references made of record, what specific understanding would have suggested the combination of references. Instead, the obviousness analysis in the Office Action is limited to a discussion of how the references can be pieced together to yield the claimed invention. As the Federal Circuit stated in *Interconnect Planning Corp. v. Feil*, 774 F.2d 1132, 227 U.S.P.Q. 543 (Fed. Cir. 1985):

It is an error to reconstruct the patentee's claimed invention from the prior art by using the patentee's claim as a "blueprint." When prior art references require selective combination to render obvious a subsequent invention, there must be some reason for the combination other than the hindsight obtained from the invention itself.

To believe that one skilled in the art would be motivated to employ applicant's disclosed methods, when Urao and Gordon-Kamm, either alone or in combination, never even discuss, suggest, or mention a reason for expressing a gene encoding a DNA molecule encoding a polypeptide that includes a PK domain as claimed by applicant, is to assume

a level of inspiration constituting inventive activity. The case law makes clear that to avoid a hindsight-based obviousness analysis the Patent Office bears the burden of elucidating factual teachings, suggestions, or incentives from the prior art that show the suitability of the combination of references. *See Graham v. John Deere Co.*, 383 U.S. 1, 18, 148 U.S.P.Q. 459, 467 (1966) (“strict observance” of factual predicates to obviousness conclusion required).

Applicant also notes the Office’s assertion that the claimed transgenic plants “are expected to be tolerant of stresses such as salt, dehydration, and temperature because the mechanisms of resistance to these stresses share many common pathways.” This position, however, is unavailing because this is an inappropriate standard for obviousness. As held by the Federal Circuit, “[i]nherency and obviousness are distinct concepts.” *W. L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 1555, 220 U.S.P.Q. 303, 314 (Fed. Cir. 1983) (citing *In re Spormann*, 363 F.2d 444, 150 U.S.P.Q. 449, 452 (1966)), *cert. denied*, 469 U.S. 852, 105 S.Ct.172 (1984). *See also In re Oelrich*, 666 F.2d 578, 581-82, 212 U.S.P.Q. 323, 326 (C.C.P.A. 1981) (“The mere fact that a certain thing may result from a given set of circumstances is not sufficient [to establish inherency.]”) (citations omitted) (emphasis added); and *In re Spormann*, 363 F.2d 444, 448, 150 U.S.P.Q. 449, 452 (“That which may be inherent is not necessarily known. Obviousness cannot be predicated on what is unknown.”). The Office’s retrospective view of inherency of the claimed invention is not a substitute for a teaching or suggestion supporting an obviousness rejection, and, for this reason as well, the § 103

rejection should be withdrawn.

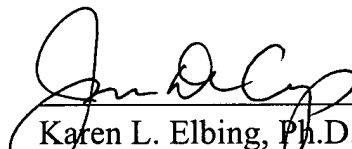
CONCLUSIONS

Applicant submits that the claims are now in condition for allowance, and such action is respectfully requested. Enclosed is a petition to extend the period for replying for three months, to and including April 14, 2000.

If there are any charges, or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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